

Metabolic syndrome and 5-year incident hyperuricemia among older Chinese adults: a community-based cohort study

Jing-Hong Liu

School of Public Health, Medical College of Soochow University, Suzhou

Qing-Hua Ma

The 3rd People's Hospital of Xiangcheng District, Suzhou

Yong Xu

School of Public Health, Medical College of Soochow University, Suzhou

Xing Chen (✉ cx1708@126.com)

Department of Children Health Care, Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou

Chen-Wei Pan (✉ pcwonly@gmail.com)

Medical College of Soochow University

Research

Keywords: Hyperuricemia, metabolic syndrome, older adults, epidemiology

Posted Date: August 24th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-62307/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy on November 1st, 2020. See the published version at <https://doi.org/10.2147/DMSO.S278542>.

Abstract

Background

There was a lack of studies focusing on older adults about the longitudinal association between metabolic syndrome (MetS) and hyperuricemia (HUA). We aimed to assess the association of baseline MetS and incident HUA among older Chinese adults, with a special focus on the associations between different combinations of MetS components and HUA.

Methods

Data of 3,247 Chinese adults aged 60 years or older included in a community-based longitudinal cohort study were analyzed. Anthropometric examinations and collection of blood sample were conducted both at baseline and follow-up. HUA was defined as 7 mg/dl or above for men and 6 mg/dl or greater for women. MetS was assessed based on the National Cholesterol Education Program-Adult Treatment Panel \AA , and older adults with presence of at least three of MetS components were considered as having MetS.

Results

MetS and its components including high blood pressure (BP), high body mass index, diabetes mellitus and high triglycerides were significantly related to incident HUA. The association between high BP and incident HUA is strongest among the five MetS components. Among all combinations of MetS components, the group consisting of diabetes mellitus, high BP and high triglycerides had the highest odds for incident HUA (OR = 13.07, 95%CI = 4.95–34.54).

Conclusions

MetS and its components except for low high-density lipoprotein cholesterol could increase the risk of HUA among community-dwelling older adults and high BP may be the most important determinant.

Background

Hyperuricemia (HUA), an important risk factor for gout [1], is a worldwide public health problem with high prevalence across different ethnic groups [2, 3]. The prevalence of HUA increased with age and was higher among older adults [4, 5]. HUA could increase the risk of cardiovascular events and all-cause mortality [6], and therefore understanding the risk factors for HUA is important for the prevention of gout and cardiovascular events. Specific metabolic abnormalities such as blood glucose [7], pressure [8] and lipids [9] have been suggested to be involved in the development of HUA. Metabolic syndrome (MetS) is a constellation of major metabolic disorders and understanding its association with HUA could more

comprehensively and accurately evaluate how metabolic abnormalities plays a role in the pathological mechanism of HUA.

The prevalence of HUA was higher in MetS when compared to those without MetS [10], and serum uric acid (SUA) was also reported to be increased in individuals with MetS [11, 12]. Moreover, studies assessing the longitudinal associations between MetS and SUA/HUA indicated that MetS could predict elevated SUA or incident HUA [13, 14]. However, some key questions remain unanswered. First, there was a lack of studies focusing on older adults, who have a high prevalence and incidence of both conditions compared with younger generations. Second, MetS includes 5 major components and which combination of these components best predicts the incidence of HUA has not been elucidated.

To address this gap, we performed a community-based longitudinal cohort study to assess the association of baseline MetS and incident HUA among Chinese adults aged 60 years or older, with a special focus on the associations between different combinations of MetS components and the occurrence of HUA. The findings would be conducive to tackling modifiable risk factors for the prevention of HUA and gout.

Methods

Study Design and Procedure

This was a community-based cohort study, which was conducted among older adults aged 60 years or older lived in Weitang town of Suzhou located in the east part of China. Details of the baseline study have been described elsewhere [15-17]. In the baseline examinations, 6,030 families who had older adult aged 60 years or older based on local official records received an invitation letter, which explain the nature of the study and invite the older adults to participate. Exclusion criteria applied to those whom had been living there shorter than six months, had migrated from the residing address, or deceased. Of the 5,613 eligible older adults, 4,611 attended the baseline clinical examinations from August 2014 to February 2015. The final sample at baseline consisted of 4,579 older adults who had complete data of anthropometric examinations, questionnaires and blood sample analyses. Five years later, these participants were invited to attend the anthropometric examination and collected of blood sample. Home visits or revisits were conducted to encourage older adults who did not participant in the follow-up examinations to attend with the aim of improving the follow-up rate of study. Older adults at baseline were excluded when he or she declined to participant, moved away and could not be contacted or deceased before the follow-up examination. Older adults with HUA at baseline or without data about SUA at follow-up examination were excluded. Official death registration forms were used to identify the death of individuals at baseline.

Both baseline and follow-up studies were conducted abide by the tenets of the Helsinki Declaration and were approved by the Institutional Review Board of Soochow University.

Clinical and biochemical measurements

Blood samples of participants were collected and frozen at -80°C before transferring to laboratory technicians for achieving related data including SUA, fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C) and blood triglycerides.

Blood pressure (BP) was measured using automatic blood pressure monitor (Dinamap model Pro Series DP110X-RW, 100V2; GE Medical Systems Information Technologies, Inc., Milwaukee, Wisconsin, United States) when older adults had a rest of 5 minutes or longer. The recorded BP was average value of the last two readings. Body height and weight of older adults without shoes and with light clothing were measured using a wall-mounted measurement tape and digital scale, separately. Body mass index (BMI, kg/m²) was calculated as the weight in kilograms divided by the square of the height in meters.

These clinical and biochemical indicators were examined with similar procedures for both baseline and follow-up studies participants.

Definitions of HUA and MetS

HUA was defined as 7 mg/dl or above for men and 6 mg/dl or greater for women [18].

MetS of participants were assessed based on the National Cholesterol Education Program-Adult Treatment Panel III [19]. MetS was diagnosed when participants met three or more of following components: (1) BMI of 25 kg/m² or above; (2) high BP (BP of 130/85 mmHg or greater or on antihypertensive drug treatment); (3) elevated blood triglycerides (1.7 mmol/L or higher); (4) diabetes mellitus defines as FPG of 7.0 mmol/L or above or with diabetes; (5) low HDL-C (lower than 1.0 mmol/L in men and 1.3 mmol/L in women).

Assessment of main covariates

Information on participants' socio-demographic characteristics including age, gender, marriage status (living with spouse/living without spouse), educational level (primary and below education/ secondary education or above) and monthly income (\leq 1000/1001-3000/ $>$ 3000 Chinese Yuan) as well as lifestyle habits was collected using a pre-designed questionnaire. Data regarding lifestyle habits such as smoking, alcohol intake, tea consumption and physical activity were also collected during the questionnaire interview.

Statistics analysis

Chi-square test and student's t-test were separately used to compare categories and continuous variables of participants according to HUA status at follow-up, and percentage as well as mean \pm standard deviation were calculated to express the comparison, as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using two logistic regression models to estimate the effects of baseline MetS and its components on 5-year incident HUA. The first model adjusted for age and gender only, and the second one additionally adjusted for marriage status, educational level, monthly income, lifestyle habits including alcohol intake, smoking status, tea consumption, physical activity and baseline

SUA. In addition, in logistic regressions of assessing linear trends, quartiles of MetS components at baseline were treated as continuous variables by assigning each quartile with a median. Logistic regression model was also used to investigate the influences of different combinations of baseline MetS components on incident HUA and those without any MetS components were treated as “reference group”. A stratified-analysis was performed to evaluate the associations of baseline MetS components with incident HUA in different statuses of diabetes mellitus component.

Data were analyzed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) and statistical significance was considered if a p-value was less than 0.05.

Results

Among 4,579 older adults at baseline, 183 (4.0%) deceased before the follow-up examination and 526 (11.5%) refused to participant or were out of touch. Of the 3,870 participants enrolled in the follow-up examination, 608 older adults with HUA at baseline and 15 participants without data about SUA at follow-up examination were excluded. Eventually, 3,247 older adults were included in this longitudinal analysis.

This study sample consisted of 1,517 men and 1,730 women with respective average SUA of 5.4 mg/dl and 4.4 mg/dl at baseline. Totally, 308 (9.5%) developed HUA among 3,247 participants free of HUA at baseline. As shown in Fig. 1, incidence of HUA increased with elevated number of MetS components in both men and women (both p values for trend < 0.001). In participants with MetS, the incidence of HUA is similar in men and women (17.0% versus 16.3%). Participants’ characteristics by HUA status at follow-up are displayed in **Table 1**. Compared to participants without HUA at follow-up, older adults with HUA were more likely to have higher level of SBP, DBP, BMI, FPG, TG and lower level of HDL-C.

Table 1. Baseline characteristics of study participants according to development of hyperuricemia

Characteristic	No HUA (n=2939)	HUA (n=308)	P value
Age, mean(SD), years	66.9(5.5)	67.5(5.8)	0.09
Gender (women), n (%)	1565(53.2)	165(53.6)	0.91
Primary and below education, n (%)	2554(86.9)	272(88.3)	0.48
Living with spouse, n (%)	2470(84.0)	256(83.1)	0.67
Monthly income			0.39
≤1000 CNY	1628(55.4)	181(58.8)	
1001-3000 CNY	1100(37.4)	103(33.4)	
>3000 CNY	211(7.2)	24(7.8)	
Current smoking, n (%)	763(26.0)	80(26.0)	0.77
Alcohol consumption, n (%)	629(21.4)	76(24.7)	0.19
Tea consumption, n (%)	964(32.8)	108(35.1)	0.42
Physical activity, n (%)	1231(41.9)	127(41.4)	0.86
SBP, mean(SD), mmHg	143.2(19.3)	148.2(19.4)	<0.001
DBP, mean(SD), mmHg	85.2(11.2)	87.2(11.5)	0.003
BMI, mean(SD), kg/m ²	23.2(5.0)	24.3(2.7)	<0.001
FPG, mean(SD), mmol/L	5.6(1.1)	5.8(1.3)	0.001
HDL-C, mean(SD), mmol/L	1.5(0.4)	1.4(0.4)	<0.001
TG, mean(SD), mmol/L	1.3(0.7)	1.6(0.9)	<0.001

HUA, hyperuricemia; *SD*, standard deviation; *CNY*, Chinese Yuan; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *BMI*, body mass index; *FPG*, fasting plasma glucose; *HDL-C*, high-density lipoprotein cholesterol; *TG*, triglycerides

Table 2 displays linear trends between baseline MetS components and risk of HUA. Older adults in the 4th quartiles of systolic BP, BMI, FPG and triglycerides had a greater risk of developing HUA compared to those in first quartiles ($P < 0.05$). Even after adjusting for socio-demographic characteristics, lifestyle habits and baseline SUA, elevated quartiles of MetS components except diastolic BP and HDL-C quartiles were associated with an increasing risk of HUA (all p values for trend < 0.05). MetS (OR = 1.73, $P < 0.001$)

and its components including high BP (OR = 2.16, P = 0.002), high BMI (OR = 1.87, P < 0.001), diabetes mellitus (OR = 1.76, P = 0.002) and high triglycerides (OR = 1.44, P = 0.01) were significantly related to incident HUA. The association between high BP and incident HUA is strongest among the five MetS components (Table 3). Moreover, increasing number of MetS components at baseline was positively related to incident HUA though the presence of only one MetS component was not a significant predictor.

Table 2

Odds ratios and 95% confidence intervals for the risk of hyperuricemia according to quartiles of metabolic syndrome components

Characteristics	Age, Sex-Adjusted Model		Multivariable-Adjusted Model*	
	OR(95%CI)	P value for trend	OR(95%CI)	P value for trend
SBP quartiles, mmHg		< 0.001		0.01
1 (\leq 130)	1.00		1.00	
2 (131–143)	1.24(0.86,1.79)		1.08(0.73,1.59)	
3 (144–156)	1.59(1.12,2.27)		1.35(0.92,1.96)	
4 (\geq 156)	1.85(1.31,2.62)		1.51(1.04,2.19)	
DBP quartiles, mmHg		0.003		0.18
1 (\leq 78)	1.00		1.00	
2 (79–85)	1.21(0.86,1.72)		0.99(0.68,1.44)	
3 (86–93)	1.35(0.96,1.90)		1.10(0.76,1.59)	
4 (\geq 93)	1.63(1.17,2.28)		1.24(0.87,1.78)	
BMI quartiles, kg/m²		< 0.001		< 0.001
1 (\leq 21.91)	1.00		1.00	
2 (21.92–23.42)	1.61(1.09,2.37)		1.36(0.90,2.04)	
3 (23.43–24.09)	1.83(1.22,2.73)		1.45(0.94,2.23)	
4 (\geq 24.09)	3.20(2.23,4.61)		2.15 (1.45,3.17)	
FPG, mmol/L		0.001		0.01
1 (\leq 4.98)	1.00		1.00	
2 (4.99–5.35)	1.20(0.84,1.71)		1.25(0.86,1.83)	
3 (5.36–5.83)	1.29(0.90,1.83)		1.28(0.88,1.87)	
4 (\geq 5.83)	1.73(1.24,2.42)		1.61(1.12,2.31)	

SBP, systolic blood pressure; *DBP*, diastolic blood pressure; *BMI*, body mass index; *FPG*, fasting plasma glucose; *HDL-C*, high-density lipoprotein cholesterol; *TG*, triglycerides; *OR*, odds ratio; *CI*, confidence interval

*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid

Characteristics	Age, Sex-Adjusted Model		Multivariable-Adjusted Model*	
	OR(95%CI)	P value for trend	OR(95%CI)	P value for trend
HDL-C, mmol/L		< 0.001		0.05
1 (≤ 1.20)	1.00		1.00	
2 (1.21–1.43)	0.66(0.48,0.90)		0.73(0.52,1.02)	
3 (1.44–1.71)	0.61(0.44,0.83)		0.81(0.58,1.15)	
4 (≥ 1.71)	0.45(0.31,0.63)		0.66(0.45,0.96)	
TG, mmol/L		< 0.001		< 0.001
1 (≤ 0.83)	1.00		1.00	
2 (0.84–1.12)	1.15(0.76,1.71)		0.96(0.63,1.47)	
3 (1.13–1.55)	2.01(1.39,2.90)		1.45(0.98,2.14)	
4 (≥ 1.55)	2.93(2.06,4.17)		1.79(1.22,2.61)	
<i>SBP</i> , systolic blood pressure; <i>DBP</i> , diastolic blood pressure; <i>BMI</i> , body mass index; <i>FPG</i> , fasting plasma glucose; <i>HDL-C</i> , high-density lipoprotein cholesterol; <i>TG</i> , triglycerides; <i>OR</i> , odds ratio; <i>CI</i> , confidence interval				
*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid				

Table 3
Risk of developing hyperuricemia according to metabolic syndrome and its components

Characteristics	Age, Sex-Adjusted Model		Multivariable-Adjusted Model*	
	OR(95%CI)	P value	OR(95%CI)	P value
MetS				
Absent	1.00		1.00	
Present	2.43(1.87,3.16)	< 0.001	1.73(1.30,2.30)	< 0.001
High BP component				
Absent	1.00		1.00	
Present	2.76(1.73,4.39)	< 0.001	2.16(1.33,3.50)	0.002
High BMI component				
Absent	1.00		1.00	
Present	2.44(1.88,3.17)	< 0.001	1.87(1.41,2.47)	< 0.001
Diabetes mellitus component				
Absent	1.00		1.00	
Present	1.65(1.19,2.28)	0.003	1.76(1.23,2.52)	0.002
Low HDL-C component				
Absent	1.00		1.00	
Present	1.73(1.31,2.27)	< 0.001	1.23(0.92,1.66)	0.17
High TG component				
Absent	1.00		1.00	
Present	1.98(1.53,2.57)	< 0.001	1.44(1.08,1.90)	0.01
Number of MetS components				
0	1.00		1.00	
1	1.77(1.00,3.14)	0.05	1.41(0.78,2.55)	0.26

MetS, metabolic syndrome; *BP*, blood pressure; *BMI*, body mass index; *HDL-C*, high-density lipoprotein cholesterol; *TG*, triglycerides; *OR*, odds ratio; *CI*, confidence interval

*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid

Characteristics	Age, Sex-Adjusted Model		Multivariable-Adjusted Model*	
	OR(95%CI)	P value	OR(95%CI)	P value
2	3.48(1.96,6.19)	< 0.001	2.38(1.31,4.34)	0.005
3	4.73(2.60,8.60)	< 0.001	2.70(1.44,5.07)	0.002
4+	6.80(3.51,13.17)	< 0.001	3.57(1.77,7.18)	< 0.001
<i>MetS</i> , metabolic syndrome; <i>BP</i> , blood pressure; <i>BMI</i> , body mass index; <i>HDL-C</i> , high-density lipoprotein cholesterol; <i>TG</i> , triglycerides; <i>OR</i> , odds ratio; <i>CI</i> , confidence interval				
*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid				

Table 4 presents the associations of specific combinations of MetS components at baseline with incident HUA. In this analysis, individuals free of MetS components were treated as “reference group” and we found that the presence of single MetS component had no influence on incident HUA. In combinations of two MetS components, groups of diabetes mellitus and high BP (2.1), high BP and high BMI (2.5), high BP and high triglycerides (2.6) as well as high BP and low HDL-C (2.7) were significantly related to incident HUA (all p values < 0.05). Groups including both high BP and other two MetS components were associated with higher risk of incident HUA (3.1, 3.2, 3.3, 3.7, 3.8, 3.9). Combination of four MetS components without high triglycerides was not significantly linked to incidence of HUA while other four combinations showed significant associations. Participants with all five MetS components were associated with approximately five-fold odds of incident HUA (OR = 5.01, 95%CI = 1.31–19.26). Among all combinations of MetS components, the group consisting of diabetes mellitus, high BP and high triglycerides had the highest odds for incident HUA (OR = 13.07, 95%CI = 4.95–34.54). All combinations of MetS associated with incident HUA contained the component of high BP.

Table 4

Associations between individual and specific combinations of metabolic syndrome components and risk of hyperuricemia

Metabolic syndrome components					Hyperuricemia		
Diabetes mellitus	High BP	High BMI	High TG	Low HDL-C	Age, sex-adjusted OR(95%CI)	P value	
Absence of any components of MetS							
1					1.00		
Individual component of MetS							
1	√				1.69(0.21, 13.68)	0.62	
2		√			1.77(1.00, 3.14)	0.05	
3			√		3.58(0.95, 13.42)	0.06	
4				√	1.44(0.18, 11.54)	0.73	
5					√	---	
Combination of two components of MetS							
1	√	√			3.20(1.50, 6.83)	0.003	
2	√		√		---		
3	√			√	---		
4	√				√	8.11(0.79, 83.73)	0.08
5		√	√			4.55(2.41, 8.61)	< 0.001
6		√		√		2.77(1.34, 5.71)	0.01
7		√			√	3.50(1.75, 7.00)	< 0.001
8			√	√		---	
9			√		√	---	
10				√	√	---	

BP, blood pressure; *BMI*, body mass index; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol; *MetS*, metabolic syndrome

Metabolic syndrome components						Hyperuricemia	
Combination of three components of MetS							
1	✓	✓	✓			3.07(1.05, 8.96)	0.04
2	✓	✓		✓		13.07(4.95, 34.54)	< 0.001
3	✓	✓			✓	3.29(1.02, 10.66)	0.05
4	✓		✓	✓		---	
5	✓		✓		✓	---	
6	✓			✓	✓	---	
7		✓	✓	✓		6.77(3.06, 15.02)	< 0.001
8		✓	✓		✓	5.40(2.37, 12.28)	< 0.001
9		✓		✓	✓	3.58(1.76, 7.29)	< 0.001
10			✓	✓	✓	---	
Combination of four components of MetS							
1	✓	✓	✓	✓		11.54(3.52, 37.79)	< 0.001
2	✓	✓	✓		✓	1.63(0.20, 13.20)	0.65
3	✓	✓		✓	✓	4.29(1.54, 11.94)	0.01
4	✓		✓	✓	✓	---	
5		✓	✓	✓	✓	9.48(4.42, 20.34)	< 0.001
Combination of all five components of MetS							
1	✓	✓	✓	✓	✓	5.01(1.31, 19.26)	0.02
<i>BP</i> , blood pressure; <i>BMI</i> , body mass index; <i>TG</i> , triglycerides; <i>HDL-C</i> , high-density lipoprotein cholesterol; <i>MetS</i> , metabolic syndrome							

In stratified analysis by the presence of diabetes mellitus, high BP (OR = 3.17, 95%CI = 1.30–3.61), high BMI (OR = 2.06, 95%CI = 1.52–2.80) and low HDL-C (OR = 1.39, 95%CI = 1.00-1.92) increased risk of HUA

only in participants without diabetes mellitus. (Table 5)

Table 5
Associations between components of metabolic syndrome and risk of hyperuricemia by status of diabetes mellitus component

Components of MetS	With diabetes mellitus component		Without diabetes mellitus component	
	Multivariable-Adjusted* OR(95%CI)	P value	Multivariable-Adjusted* OR(95%CI)	P value
High BP	1.02(0.20, 5.26)	0.98	2.17(1.30, 3.61)	0.003
High BMI	1.03(0.48, 2.20)	0.95	2.06(1.52, 2.80)	< 0.001
High TG	1.97(0.99, 3.90)	0.05	1.30(0.94, 1.78)	0.11
Low HDL-C	0.51(0.24, 1.11)	0.09	1.39(1.00, 1.92)	0.05
<i>MetS</i> , metabolic syndrome; <i>BP</i> , blood pressure; <i>BMI</i> , body mass index; <i>TG</i> , triglycerides; <i>HDL-C</i> , high-density lipoprotein cholesterol				
*Adjusted for age, sex, educational level, monthly income, marriage status, smoking status, alcohol intake, tea consumption, physical activity and baseline serum uric acid				

Discussion

This community-based cohort study among older Chinese adults aged 60 years or older indicated that MetS and its components of diabetes mellitus, high BP, high BMI and high triglycerides at baseline were associated with incident HUA. In addition, high BP may be the most important MetS component contributing to incidence of HUA. Older adults with simultaneous high BP, diabetes mellitus and high triglycerides may be most likely to develop HUA among all possible combinations of MetS components.

The result that baseline MetS as a risk factor for incident HUA was not unexpected and was consistent with some studies carried out in other countries [13, 14, 20]. A cohort study in middle-aged men in South Korea demonstrated that the incidence of HUA increased across MetS at baseline with the hazard ratio of being 1.41 [13]. In studies conducted in North American countries, MetS was reported to be associated with incident HUA both in men and women [14, 20]. Moreover, a study with participants from three urban areas and one rural county of Beijing showed a 2.0-fold risk of HUA among community elderly with MetS [21], which was similar to our results.

It was in line with some studies that MetS components of high BP, high BMI, diabetes mellitus and high triglycerides at baseline were related to increased risk of HUA [20, 22]. In this study, 96.6% older adults were found having abnormal BP defined as 130/85 mmHg or greater among individuals suffered from MetS. High BP component may act as an important risk factor related to the incidence of HUA in this population. A longitudinal study has reported that those with hypertension were at a 1.65-fold risk of HUA

[22]. Hypertension may result in the vascular disease related to decreased renal blood flow and finally stimulate urate reabsorption [23]. The other processes of hypertension cause HUA may through blocking urate excretion [24] and generating increased xanthine oxidase associated with production of uric acid [8, 25]. In our study, high BMI also had a higher impact on incident HUA. According to a study conducted among large cohorts, the increment of risk of HUA was 7.5% when per 4 kg/m² increased in BMI [26]. Insulin resistance may be a linkage between obesity and HUA. Obesity may through chronic adipose tissue inflammation to cause the insulin resistance [27], which may lead to the enhanced activity of hexose monophosphate shunt and eventually contribute to increased purine biosynthesis and turnover [28]. Moreover, higher serum leptin concentration in individuals with obesity could induce oxidative stress in endothelial cells [29, 30]. The oxidative stress has been reported to be associated with increased SUA concentration [30].

Findings of our study added the evidence to the impact of MetS and its components at baseline on incident HUA. It has been reported that programmed HUA intervention could optimize their cardiovascular lesions [31]. Combination of high BP, diabetes mellitus and high triglycerides was associated with highest risk of incident HUA among all possible combinations of MetS components. This result may help to identify community-dwelling older adults at high risk of developing HUA and take measures to prevent HUA through modifying these common diseases among older adults. In addition, realizing the importance of MetS on incident HUA may be beneficial to make intervention and clinical management of MetS as well as HUA, which may eventually reduce the risk of HUA-related cardiovascular events.

The strengths of this study included community-based sample, longitudinal design, reasonable follow-up rate and sufficient numbers of individuals with incident HUA. However, there were also several limitations, which should be noted. First, although we have adjusted a wide range of confounders, residual confounding may still exist. For example, dietary habits might have an impact on SUA levels. Consumption of purine-rich foods like seafood may increase SUA levels [32] but information on this issue was not collected in this study. Second, the underascertainment and misclassification of outcome measure are possible because the incident cases might have been underestimated. Information on antihyperuricemia medication intake had been collected but few reported. Recall bias or social desirability bias may lead to the underestimation of the incidence of HUA and distort on the association of MetS and its components at baseline with incident HUA.

Conclusions

In conclusion, MetS and its components such as high BP, high BMI, diabetes mellitus and high triglycerides could increase the risk of HUA among community-dwelling older adults and high BP may be the most important determinant. Combination of high BP, diabetes mellitus and high triglycerides best predicts incident HUA. Additional studies are needed to confirm the findings in other ethnic groups and to further investigate the underlying mechanisms for the association. Randomized controlled trials are also warranted to investigate whether lowering BP in hypertensive patients or losing weight in obese populations could reduce the risk of HUA among the elderly.

Abbreviations

MetS: metabolic syndrome; Hyperuricemia: HUA; BP: blood pressure; Serum uric acid : SUA; FPG: fasting plasma glucose; HDL-C: high-density lipoprotein cholesterol; BMI: body mass index; OR: odds ratio; CI: confidence interval.

Declarations

Ethics approval and consent to participate: The study adhered to the Declaration of Helsinki and ethics approval was obtained from the Institutional Review Board of the Soochow University. Written informed consent was obtained from each participant at the recruitment stage of the study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets analyzed in this study are available from the corresponding author (Chen-Wei Pan, pcwonly@gmail.com) upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This study was supported by the Science and Technology Bureau of Xiangcheng District in Suzhou, China under grant no. XJ201706 and the Health Commission of Suzhou under grant no. GSWS2019090.

Authors' contributions: JHL conducted the statistical analyses and wrote manuscript. QHM and YX contributed data collection and interpretation of the data. CWP and XC conceived and designed the study and revised manuscript. All authors read and approved the final manuscript.

Acknowledgments: Not Applicable

References

1. Dalbeth N, Merriman TR, Stamp LK: Gout. *Lancet*. 2016;388(10055):2039–52.
2. Zhu Y, Pandya BJ, Choi HK: **Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007–2008.** *Arthritis and rheumatism* 2011, **63**(10):3136–3141.
3. Liu H, Zhang XM, Wang YL, Liu BC. Prevalence of hyperuricemia among Chinese adults: a national cross-sectional survey using multistage, stratified sampling. *J Nephrol*. 2014;27(6):653–8.
4. Kumar AUA, Browne LD, Li X, Adeeb F, Perez-Ruiz F, Fraser AD, Stack AG. Temporal trends in hyperuricaemia in the Irish health system from 2006–2014: A cohort study. *PloS one*. 2018;13(5):e0198197.
5. Wu J, Qiu L, Cheng XQ, Xu T, Wu W, Zeng XJ, Ye YC, Guo XZ, Cheng Q, Liu Q, et al. Hyperuricemia and clustering of cardiovascular risk factors in the Chinese adult population. *Scientific reports*.

- 2017;7(1):5456.
6. Chen PH, Chen YW, Liu WJ, Hsu SW, Chen CH, Lee CL. **Approximate Mortality Risks between Hyperuricemia and Diabetes in the United States.** *Journal of clinical medicine* 2019, 8(12).
 7. Andrade JA, Kang HC, Greffin S, Garcia Rosa ML, Lugon JR. Serum uric acid and disorders of glucose metabolism: the role of glycosuria. *Brazilian journal of medical biological research = Revista brasileira de pesquisas medicas e biologicas.* 2014;47(10):917–23.
 8. Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: an active component or an innocent bystander? *Metab Clin Exp.* 2006;55(10):1293–301.
 9. Tinahones JF, Perez-Lindon G, FJ CS, Pareja A, Sanchez-Guijo P, Collantes E. Dietary alterations in plasma very low density lipoprotein levels modify renal excretion of urates in hyperuricemic-hypertriglyceridemic patients. *J Clin Endocrinol Metab.* 1997;82(4):1188–91.
 10. Kang WM, Zhang JS, Wang MS, Gu YC, Yu JC. **Prevalence of metabolic syndrome and its associations with other metabolic disorders and cardiovascular changes in health examination population in Beijing.** *Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih* 2009, 24(4):227–230.
 11. Numata T, Miyatake N, Wada J, Makino H. Comparison of serum uric acid levels between Japanese with and without metabolic syndrome. *Diabetes Res Clin Pract.* 2008;80(1):e1–5.
 12. Stiburkova B, Pavlikova M, Sokolova J, Kozich V. Metabolic syndrome, alcohol consumption and genetic factors are associated with serum uric acid concentration. *PloS one.* 2014;9(5):e97646.
 13. Ryu S, Chang Y, Zhang Y, Kim SG, Cho J, Son HJ, Shin H, Guallar E. A cohort study of hyperuricemia in middle-aged South Korean men. *Am J Epidemiol.* 2012;175(2):133–43.
 14. Muntner P, Srinivasan S, Menke A, Patel DA, Chen W, Berenson G. Impact of childhood metabolic syndrome components on the risk of elevated uric acid in adulthood: the Bogalusa Heart Study. *Am J Med Sci.* 2008;335(5):332–7.
 15. Yang XJ, Tian S, Ma QH, Sun HP, Xu Y, Pan CW. **Leukocyte-related parameters in older adults with metabolic syndrome.** *Endocrine* 2020.
 16. Liu JH, Qian YX, Ma QH, Sun HP, Xu Y, Pan CW. Depressive symptoms and metabolic syndrome components among older Chinese adults. *Diabetol Metab Syndr.* 2020;12:18.
 17. Qian YX, Liu JH, Ma QH, Sun HP, Xu Y, Pan CW. Associations of sleep durations and sleep-related parameters with metabolic syndrome among older Chinese adults. *Endocrine.* 2019;66(2):240–8.
 18. Roubenoff R. Gout and hyperuricemia. *Rheum Dis Clin North Am.* 1990;16(3):539–50.
 19. Executive **Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III).** *Jama* 2001, 285(19):2486–2497.
 20. Rivera-Paredes B, Macias-Kauffer L, Fernandez-Lopez JC, Villalobos-Comparan M, Martinez-Aguilar MM, de la Cruz-Montoya A, Ramirez-Salazar EG, Villamil-Ramirez H, Quiterio M, Ramirez-Palacios P,

et al: **Influence of Genetic and Non-Genetic Risk Factors for Serum Uric Acid Levels and Hyperuricemia in Mexicans.** *Nutrients* 2019, 11(6).

21. Lu X, Li X, Zhao Y, Zheng Z, Guan S, Chan P. Contemporary epidemiology of gout and hyperuricemia in community elderly in Beijing. *Int J Rheum Dis.* 2014;17(4):400–7.
22. McAdams-DeMarco MA, Law A, Maynard JW, Coresh J, Baer AN. Risk factors for incident hyperuricemia during mid-adulthood in African American and white men and women enrolled in the ARIC cohort study. *BMC Musculoskelet Disord.* 2013;14:347.
23. Messerli FH, Frohlich ED, Dreslinski GR, Suarez DH, Aristimuno GG. Serum uric acid in essential hypertension: an indicator of renal vascular involvement. *Ann Intern Med.* 1980;93(6):817–21.
24. Puig JG, Ruilope LM. Uric acid as a cardiovascular risk factor in arterial hypertension. *Journal of hypertension.* 1999;17(7):869–72.
25. Friedl HP, Till GO, Trentz O, Ward PA. Role of oxygen radicals in tourniquet-related ischemia-reperfusion injury of human patients. *Klinische Wochenschrift.* 1991;69(21–23):1109–12.
26. Palmer TM, Nordestgaard BG, Benn M, Tybjaerg-Hansen A, Davey Smith G, Lawlor DA, Timpson NJ. Association of plasma uric acid with ischaemic heart disease and blood pressure: mendelian randomisation analysis of two large cohorts. *BMJ.* 2013;347:f4262.
27. Zatterale F, Longo M, Naderi J, Raciti GA, Desiderio A, Miele C, Beguinot F. Chronic Adipose Tissue Inflammation Linking Obesity to Insulin Resistance and Type 2 Diabetes. *Frontiers in physiology.* 2019;10:1607.
28. Modan M, Halkin H, Karasik A, Lusky A. Elevated serum uric acid—a facet of hyperinsulinaemia. *Diabetologia.* 1987;30(9):713–8.
29. Bedir A, Topbas M, Tanyeri F, Alvur M, Arik N. Leptin might be a regulator of serum uric acid concentrations in humans. *Japanese heart journal.* 2003;44(4):527–36.
30. Rahmouni K, Haynes WG. Endothelial effects of leptin: implications in health and diseases. *Curr Diabetes Rep.* 2005;5(4):260–6.
31. Zhu WH, Fang LZ, Chen LY, Chen ZW, Dai HL, Chen JH. [Follow-up study of programmed intervention of hyperuricemia in the prevention and treatment of cardiovascular morbid change]. *Zhonghua yi xue za zhi.* 2010;90(10):662–6.
32. Choi HK, Liu S, Curhan G. Intake of purine-rich foods, protein, and dairy products and relationship to serum levels of uric acid: the Third National Health and Nutrition Examination Survey. *Arthritis rheumatism.* 2005;52(1):283–9.

Figures

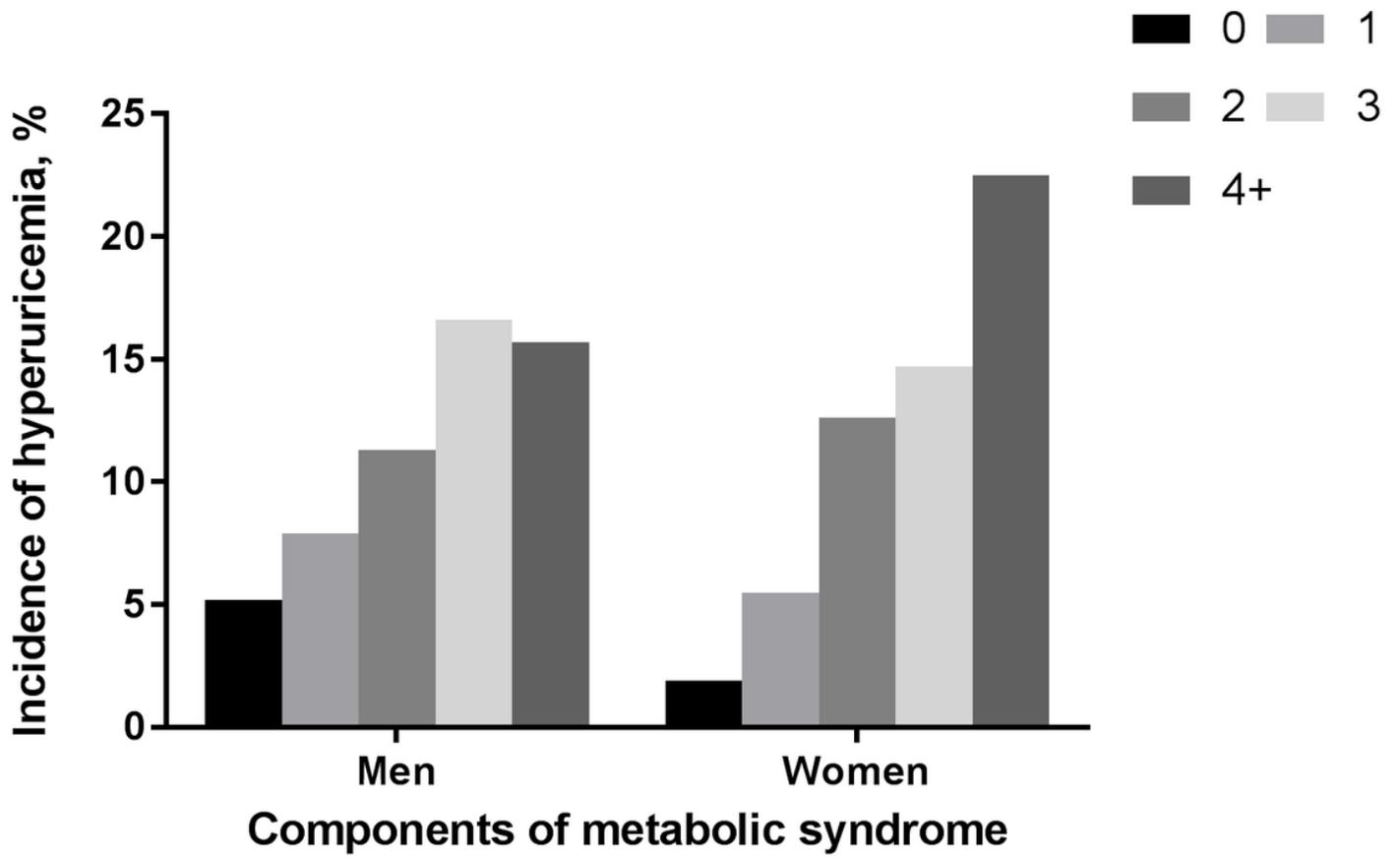


Figure 1

Incidence of hyperuricemia by increasing metabolic syndrome components in men and women.